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Merck Unveils How Its AIDS Vaccine Acts In Humans as Top Scientists Hail Studies

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SEATTLE -- For the first time, Merck & Co. has unveiled how its closely watched experimental AIDS vaccine acts in humans, and several top scientists hailed the data as "encouraging." In its presentation of early-stage data, Merck also showed how it hopes to overcome a unique challenge posed by its vaccine candidate.

A preventative vaccine is considered the only way to stop the epidemic. About 40 million people globally are estimated to be infected with HIV, the AIDS virus, and it is spreading rapidly in the poorest regions of the world.

AIDS was discovered more than two decades ago, but only one experimental HIV vaccine, made by VaxGen Inc. of Brisbane, Calif., is in large-scale human efficacy trials. Many vaccine experts consider Merck's vaccine to be the most promising candidate, based on experiments in monkeys. If the Merck vaccine should end up proving effective in people, however, it remains many years away from use in the field.

To come up with its vaccine, Merck tested many different approaches in a large, systematic series of monkey studies. Through that research Merck found that the strongest immune responses were generated by first priming the body with one kind of experimental vaccine, a "naked DNA" inoculation made of genetic material from the AIDS virus, and then boosting with a different kind of inoculation.

For the booster shot, Merck hooks an HIV gene on to a cold virus, the adenovirus, that has been genetically modified so that it cannot cause disease. In monkey studies, Merck tested several other harmless viruses as carriers, or "vectors" for the AIDS-virus gene, but found that the adenovirus carrier provoked by far the strongest immune responses.

But there is a problem: The adenovirus is so common in humans that many people have pre-existing antibodies to it. When the vaccine version of the adenovirus is injected into these people, their antibodies will attack it, just as they would a real cold virus. That could prevent the vaccine adenovirus from delivering its payload of HIV genes, rendering the whole immunization ineffective.

That is why one part of the study was particularly important. A group of trial subjects had high levels of pre-existing adenovirus antibodies -- the acid test for Merck's vaccine. These subjects also received the highest dose of the vaccine, which appeared to overcome the pre-existing antibodies in about 57% of them. In those people, the vaccine was able to induce impressive immune-system responses to HIV.

Anthony Fauci, a veteran AIDS researcher and director of the National Institute of Allergy and Infectious Diseases, said it is "dangerous to compare" vaccine studies conducted by different laboratories. But "with that caveat," he said, Merck's vaccine produced "the best immunological responses I have seen." Dr. Fauci, whose institute will work with Merck to conduct human trials of the vaccine and so is familiar with the data, said it remains to be seen whether those immune-system responses will be good enough to actually beat back the virus.

While the high-dose vaccine induced good immune responses in most of the subjects with high pre-existing antibodies, it induced only weak responses or none at all in 43%. But that didn't discourage scientists at the meeting, who pointed out that the data were very preliminary and that Merck hadn't yet deployed its vaccine in the strongest possible way.

"They have a series of modifications that could and should improve" the vaccine, said Douglas Richman, an HIV researcher at the University of California at San Diego.

Merck is counting on several strategies to increase the response rate. First, it is testing higher vaccine doses and more inoculations, which it hopes will overcome the pre-existing adenovirus antibodies. That will depend in part on whether the vaccine is tolerable. At the highest dose tested so far, the vaccine caused "moderate and sporadic malaise and body aches."

Second, it believes that the naked DNA priming inoculation also will help overcome the pre-existing antibodies, because that is what happened in its monkey studies. Merck says it hasn't yet tested the prime and booster together in humans because it is first doing separate safety tests of each vaccine type.

Third, Merck, of Whitehouse Station, N.J., plans to add more HIV genes to the vaccine, which also might prompt immune responses in more patients.

"This is an important year," Emilio Emini, Merck's head of vaccine research, said in an interview at the 9th Conference on Retroviruses and Opportunistic Infections being held this week in Seattle, where he presented the data. A year from now "is when we decide if we're going to commit" to large-scale human trials of the vaccine.

Merck's vaccine is one of a new kind of "partial protection" vaccines that don't ward off infection with the virus. Instead, the AIDS virus gains a toehold in the body, but the vaccine primes the immune system so that it keeps the virus in check, delaying or preventing the onset of full-blown AIDS. Instead of stimulating antibodies to HIV, the vaccine stimulates another arm of the immune system called "killer T-cells" because they attack and destroy cells that HIV has infected.

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